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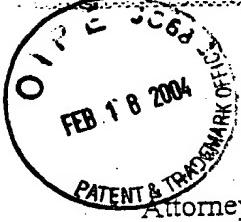
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Attorney Docket No. 9310.22CX

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.

Application Serial No: 09/463,352

Group Art Unit: 1655

Filed: January 21, 2000

Examiner: B. Sisson

For: *NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN
THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1*

MAIL STOP RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF JAAP GOUDSMIT,
PIETER OUDSHOORN, SUZANNE JURRIAANS
AND VLADIMIR VLADIMIROVICH LUKASHOV
UNDER 37 C.F.R. § 1.131

Sir:

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2. Prior to June 25, 1997, we conceived and reduced to practice the oligonucleotides having the nucleotide sequence of SEQ ID NOs 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11, respectively, as recited in the pending claims, as well as methods of use and kits employing these oligonucleotides to detect HIV-1 nucleic acid in a sample

3. In support of the above statement, we hereby submit as Appendix A a copy of relevant pages of an internal memorandum entitled "Feasability of a qualitative NASBA assay with a broad HIV-1 clade reactivity" prepared by non-inventor, F. Jacobs, under the direction of

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Jaap Goudsmit



Rijter Goudshoorn

Date

Oct 1st 2003

Date

Suzanne Jurriaans

Date

Vladimir Vladimirovich Lukashov

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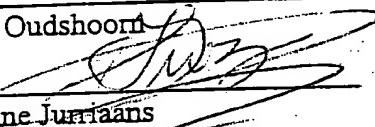
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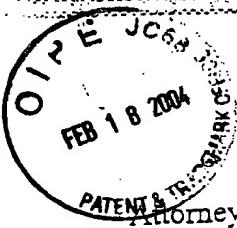

Suzanne Jurriaans

30 Oct 2003

Date

Vladimir Vladimirovich Lukashov

Date



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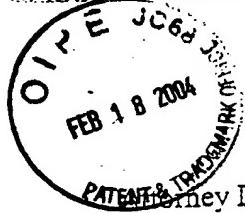
Suzanne Jurriaans

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Vladimir Vladimirovich Lukashov

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October 6, 2003



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Jaap Goudsmit

October 3, 2003
Date

Pieter Oudshoorn

Date

Suzanne Jurriaans

Date

Vladimir Vladimirovich Lukashov

Date



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Organon Teknika bv
Boxtel The Netherlands

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Author:	Name:	Date:	Signature
Department:			
NDU	F. Jacobs		

Approval:	Name:	Date:	Signature
Function:			
Groupleader	P. Oudshoom		

To be returned to R&D secretary before submitting for final approval

Final authorization:	Name:	Date:	Signature
Function:			
NDU manager	C. v. Buul		

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2. Materials and methods

2.1 Design of primers and probes.

The oligonucleotide sequences are respectively:

P1.1: aat tct aat acg act cac tat agg gAG AGG GGC GCC ACT GCT AGA GA
P1.2: aat tct aat acg act cac tat agg gAG AGG TTC GGG CGC CAC TGC TAG A
U5 end: aat tct aat acg act cac tat agg gCGGGCGCCACTGCTA
P2.1: CTG CTT AAA GCC TCA ATA AA
P2.2: CTC AAT AAA GCT TGC CTT GA

To perform ECL detection one biotin probe and two different detection probes were designed with the following sequences:

HIV-1 LTR-bio: TCT GGT AAC TAG AGA TCC CTC
HIV-LTR-AMN1: TAG TGT GTG CCC GTC TGT.
HIV-LTR-AMN2: AGT GTG TGC CCG TCT GTT.

2.2 Evaluation and optimization of the primers and probes.

The primers were tested directly in the amplification in the combinations P1.1/P2.1, P1.1/P2.2, P1.2/P2.1, P1.2/P2.2 and U5-end/P2.2 on in vitro LTR RNA and on Scott Layne RNA (subtype B, stock solution of 5.5×10^9 copies RNA/ml). The input of the RNA was 10^4 copies. The amplifications were examined on a 2% agarose gel and then blotted in 1 hour on zeta probe and cross-linked with UV. The blot was hybridized with the biotin probe (3 μ M) by incubating the blot for 4 hours at 50°C. After hybridization the blot was washed two times for 5 minutes with 3*SSC/1%SDS solution at 50°C and one time for 10 minutes with 2*SSPE/0.1%SDS solution at RT. After this the blot was incubated for 30 minutes with 2 μ l streptavidine/HRP solution (500 U/ml, Enhanced Chemiluminescence detection kit from Amersham) in 10 ml 5*SSPE/0.5%SDS. The blot was again washed two times for 5 minutes in 2*SSPE/0.1%SDS solution and one time for 10 minutes in 2*SSPE solution. The blot was dried between tissues and developed with the development solutions from the enhanced chemiluminiscense kit (Amersham). The blot was wrapped in Saran wrap and a film was placed on the blot for a couple of seconds. The film was developed according to the standard procedures.



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3.2 Evaluation of selected primers.

Figure 3. Detection of the amplimers on blot.

The primersets used were: nr 1: P1.1-P2.1, nr 2: P1.1-P2.2, nr 3: P1.2-P2.1, nr 4: P1.2-P2.2, nr 5: U5 end-5'LTRSpH1. The RNA used as input were: A: *in vitro* RNA 10⁴ copies per input, B: Scott Layne RNA 10⁴ copies per input, C: No Templates.

